REMARKS

The Specification at page 6, lines 15-18 has been amended to more clearly state that the present invention is directed, in one embodiment, to a method of detecting the presence or assessing the severity of a disease, disorder or abnormal physical state in a mammal, wherein the method includes the step of administering an effective amount of a complex-forming metal ion labeled agent, as correctly described throughout, *e.g.*, p. 4, lines 22-26; p. 15, lines 15-29. No new matter has been added.

Claims 1-31 and 33-46 were pending.

Claims 43 and 44 have been withdrawn by the Examiner as purportedly being drawn to a non-elected invention/species, the restriction having been traversed.

Claim 22 has been amended to replace the inadvertent typographical error "^{188}Rc" with the correct "^{188}Re" as described throughout the Specification, *e.g.*, p. 15, line 23.

Claim 26 has been amended to correct the term "infection" to its correct adjective form "infectious" as used to modify the word "disease." Claim 26 has additionally been corrected to include the word "degenerative" which was inadvertently omitted from the recitation of the claim, even though it was added to the claim in the *Amendment* of March 10, 2004.

Claims 38 and 40 have been amended to recite "**from** the group consisting of. . ." as appropriate for a Markush group.

New claims 47-49 have been added. Support for these claims can be found throughout the disclosure of the present application, *e.g.*, in the Specification at p. 6, lines 15-22; p. 15, line 27 to p. 16, line 20; and pending claims 26, 27 and 33. Therefore, no new matter has been added.

Claims 1-31, 33-42 and 45-49 are now pending.

I. Claims 26, 27 and 33 Satisfy 35 U.S.C. § 112, First Paragraph

Applicants note with gratitude the Examiner's removal of a number of previous rejections under 35 U.S.C. § 112.

The rejection of claims 26, 27 and 33 under 35 U.S.C. §112, ¶ 1 has been maintained in the present *Office Action*. These claims are said to be "ambiguous because one cannot ascertain what disease, disorder, abnormal physical state, oncological neurological, inflammatory, infection, degenerative disease, and other disorders, and abnormal physical states that Applicant is referring to even after reviewing the suggested area of the specification." (*Office Action*, p. 3). Further, the *Office Action* states that "[t]he claims need to be clear and concise in order for one to ascertain what disease, disorders or abnormal physical states Applicant is referring to." (*Id.*) Applicants respectfully submit that the present *Office Action* has misstated the written description standard required by 35 U.S.C. §112, ¶ 1.

Rather, the written description requirement of 35 U.S.C. §112, ¶ 1 requires only that the Specification "describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." MPEP § 2163.

The Examiner bears the burden of showing "why a person skilled in the art would not recognize that the written description of the invention provides support for the claims." MPEP §§ 2163; 2163.01. Here, the Examiner has objected to the phrase "disease, disorder or abnormal physical state." However, it is undisputed that the phrase "disease, disorder or abnormal physical state" finds support throughout the present Specification, for example, in the following:

> "The invention includes a method of detecting the presence or assessing the severity of a **disease, disorder or abnormal physical state** in a mammal

> comprising: (a) administering an agent or composition of the invention and (b) detecting the presence or assessing the severity of the **disease, disorder or abnormal physical state**. The presence or severity of the **disease, disorder or abnormal physical state** is detected or assessed with a technique selected from the group consisting of positron emission tomography, nuclear magnetic resonance imaging, scintigraphy, single photon emission computed tomography, perfusion contrast echocardiography, ultrafast X-ray computed tomography, and digital subtraction angiography."

(Specification, p. 15, line 26 to p. 16, line 5; emphasis added). The phrase, "oncological, neurological, inflammatory, infectious, and degenerative diseases" also finds support throughout the present Specification, for example, in the following:

> "The pharmaceutical compositions are used to treat diseases and provide images in **diseases, disorders or abnormal physical states including oncological, neurological, inflammatory, infection, and degenerative diseases**. Other **diseases, disorders and abnormal physical states** will be apparent to those skilled in the art and/or on review of this application or references cited in this application."

(Specification, p. 16, lines 17-20; emphasis added). Therefore, the written description requirement of 35 U.S.C. §112, ¶ 1 for claims 26, 27 and 33 has been satisfied because the term "disease, disorder or abnormal physical state" has adequate support in the Specification.

This conclusion is further supported by the concurrently filed Declaration of Karen E. Linder, PhD ("Linder Declaration"), which confirms that one skilled in the art can reasonably conclude, based on the present disclosure which discloses the invention in sufficient detail, that the inventors of U.S. Application Serial No. 09/913,401 had possession of the presently claimed invention as it relates to a method of detecting the presence or assessing the severity of an oncological, neurological, inflammatory, infectious, and degenerative disease, disorder or abnormal physical state in a mammal, as recited in claims 26 and 33 (Linder Declaration, ¶ 12).

Similarly, Dr. Linder also confirms that one skilled in the art can reasonably conclude, based on the present disclosure which discloses the invention in sufficient detail, that the inventors of U.S. Application Serial No. 09/913,401 had possession of the presently claimed invention as it relates to a method of radiotherapy of a disease, disorder or abnormal physical state in a mammal, as recited in claim 27 (Linder Declaration, ¶ 13).

Thus, it is clear that the terms that are objected to do have support in the present Specification. As such, Applicants respectfully submit that the rejection of claims 26, 27 and 33 under 35 U.S.C. §112, ¶ 1 has been overcome and should be withdrawn.

II. Claims 26, 27 and 33 Satisfy 35 U.S.C. § 112, Second Paragraph

The rejection of claims 26, 27 and 33 under 35 U.S.C. §112, ¶ 2 has been maintained; these claims are said to be ambiguous because "one cannot ascertain what disease, disorder, abnormal physical state, oncological, neurological, inflammatory, infection, degenerative disease, and other diseases, disorders, and abnormal physical states that Applicant is referring to even after reviewing the suggested areas of the specification." (*Office Action*, p. 3). Applicants respectfully traverse.

35 U.S.C. §112, ¶ 2 requires that the "specification shall conclude with one or more claims particular pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Thus, the requirements of 35 U.S.C. §112, ¶ 2 are met if: (a) the claims set forth the subject matter that Applicants regard as their invention; and (b) the claims particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. MPEP § 2171.

As is the case above with regard to 35 U.S.C. §112, ¶ 1, the language objected to

is "disease, disorder or abnormal physical state." However, Applicants respectfully submit that these terms are clear and precise enough so that one of ordinary skill in the art would be able to ascertain the metes and bounds of the claimed invention. MPEP § 2173.05. Indeed, a skilled artisan would be able to determine what conditions fall into the categories described by these terms.

This conclusion is further supported by the concurrently filed Linder Declaration, which confirms that one of ordinary skill in the art would readily understand the terms, and additionally would be able to ascertain what conditions constitute "disease, disorder or abnormal physical state" and "oncological, neurological, inflammatory, infectious, and degenerative disease, disorder or abnormal physical state." (Linder Declaration, ¶¶ 17 and 18). In fact, a search of the USPTO patents database reveals that the words "disease" or "disorder" or "abnormal physical state" are present in hundreds of issued patents in the area of pharmaceuticals and other therapeutic compositions.

Therefore, for at least these reasons, Applicants respectfully submit that claims 26, 27 and 33 satisfy the definiteness requirement of 35 U.S.C. §112 ¶ 2, and respectfully request that this rejection be reconsidered and withdrawn.

In any event, new claims 47-49 have been added to further clarify the method preambles of claims 26, 27 and 33 respectively by reciting detecting or selecting a disease from a list.

III. Applicants' Claims Are Patentable Over Sharma

Claims 1-22, 24-31, 33-42, 45 and 46 have been rejected under 35 U.S.C. § 103 as purportedly being obvious in view of U.S. Patent No. 6,027,711 to Sharma ("Sharma").

Applicants respectfully traverse for the reasons set forth below.

As an initial matter, Applicants respectfully submit that a *prima facie* case of obviousness cannot be established since Sharma fails to teach all of the limitations of the presently claimed invention. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991); MPEP §§ 2142 and 2143.

For example, Sharma does not disclose or suggest a metal support surface. Contrary to the assertion in the *Office Action*, the metal ion-binding backbone taught by Sharma is not, and cannot function as, a metal support surface as recited in Applicants' claims. The present Specification explains that a metal support surface refers to:

> "any substrate that is insoluble and inert in labeling solutions and is a metal support surface which is either made of or coated with, gold, silver or copper or a metal capable of releasably binding and coordinating sulfur or phosphorous for forming a metal complex in preparation of labeled agents. Suitable compounds that may be coated with a metal include inorganic silicate glass, alkylamino functionalized controlled-pore glass, silica or alumina beads and organic polystyrene, polyacrylamide or sugar polymers such as Sephadex and agarose."

(Specification, p. 12, lines 10-16; emphasis added).

On the other hand, Sharma teaches a metal ion-binding backbone, which is not metal, but rather is "for complexing with a metal ion" and "may be constructed of amino acids, or may be constructed such that it has available nitrogen, sulfur or oxygen atoms to complex the metal ion and may be based on metal binding chelate structures." (Sharma, col. 10, lines 9-10 and 24-28). Because such compounds are so different, and have such different properties, from the inert and insoluble metals contemplated by the present invention, the metal ion-binding backbone taught by Sharma cannot function as the metal support surface recited in the present claims. Sharma's metal ion-binding backbone is not either made of, or coated with metal, and thus is not a metal support surface as recited in the presently pending claims.

Additionally, Sharma fails to teach or suggest the limitations "a conjugate releasably bound to the support surface" and "wherein the conjugate coordinates with a complex-forming metal ion so that the labeled conjugate is released from the support surface" as recited in Applicants' claims. As the present Specification makes clear, the claimed metal support surface releasably complexes with the conjugate, allowing its release when the conjugate complexes with the metal ion. Thus, the metal ion catalyzes release of the labeled conjugate from the metal support surface upon successful labeling, resulting in solutions that are substantially free of unlabeled conjugate.

However, as discussed above, Sharma's metal ion-binding backbone complexes to the metal ion in the final metallo-construct product. In other words, there is no teaching or suggestion anywhere of a conjugate that is "releasably bound" to a metal support and that is "released" from the support surface upon complexation with a metal ion, as presently taught and claimed by Applicants.

Therefore, because Sharma fails to teach or suggest a number of the elements of Applicants' claimed invention, withdrawal of the rejection under 35 U.S.C. § 103 is respectfully requested.

Furthermore, one of ordinary skill in the art would not be motivated, based on the teachings of Sharma, to make the presently claimed invention. Specifically, there is no suggestion of a motivation in Sharma to use any support surface (let alone a metal support surface), that is releasably bound to the conjugate such that the conjugate is released when complexed to a metal ion. For example, Sharma does not disclose or suggest the advantages of using such a metal support surface or the need for improved labeling methods. Sharma also does

not disclose or teach any advantages for a releasably-bound conjugate as recited in the present claims.

Thus, there is absolutely nothing in Sharma that would motivate or suggest one of ordinary skill in the art to make the presently claimed invention. Accordingly, for at least the above reasons, it is submitted that the rejection of claims 1-22, 24-31, 33-42, 45 and 46 under 35 U.S.C. § 103 has been overcome, and Applicants respectfully request that it be withdrawn.

IV. Claim 23 is Allowable

Claim 23 has been rejected as being dependent upon a rejected base claim, but has been indicated to be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

While Applicants are grateful for the Examiner's indication, Applicants respectfully submit that in light of the present amendments and remarks, all of the presently pending claims are patentable, and that claim 23 is therefore patentable as well.

CONCLUSION

In light of the present amendments and remarks, Applicants respectfully submit that the present claims are in condition for allowance, early notice of which is earnestly sought. If any outstanding issues remain, the Examiner is invited to telephone Applicants' representatives to discuss the same.

No fees, other than the fee for extension of time to respond, are believed to be required for the filing of this *Response to Office Action*. However, please charge any additional required fees, and credit any overpayments, to Deposit Account No. 50-0540.

Respectfully submitted,

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